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| 09/842,791 | 04/27/2001 | Chihiro Uematsu | | 7893 |

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EXAMINER

WHISENANT, ETHAN C

| ART UNIT | PAPER NUMBER |
|----------|--------------|
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1634

DATE MAILED: 09/09/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Supplement 2
Office Action Summary

Application No.

09/842,791

Applicant(s)

UEMATSU ET AL.

Examiner

Ethan Whisenant, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 17 and 19-26 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 17, 19-22 and 24-26 is/are rejected.
- 7) ☒ Claim(s) 23 is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on ____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☒ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). ____.
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) ____ 6) ☐ Other: ____.

SUPPLEMENTAL DETAILED ACTION - FINAL REJECTION

1. This action is supplemental to and replaces the action mailed 06 MAY 03.

The applicant's Response (filed 27 JAN 03) has been entered. Following the entry of the claim amendments **Claim(s) 17 and 19-26** is/are pending. Rejections and/or objections not reiterated from the previous office action are hereby withdrawn. The following rejections and/or objections are either newly applied or reiterated. They constitute the complete set presently being applied to the instant application.

35 USC § 112- 2ND PARAGRAPH

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

CLAIM REJECTIONS under 35 USC § 112- 2ND PARAGRAPH

3. Claim(s) 20-22 is/are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 20 is indefinite because it is unclear what is intended by the phrase "the order of said modules in said set being different between said first module and said second module". Please clarify.

Claim 21 is indefinite because there is no nexus between the preamble and the claim steps. Claim 21 in its preamble direct to a method which is to accomplish a particular goal. However, none of the claim steps states that this goal is accomplished. For clarity, claimed methods should recite that the purpose of the method has been attained (i.e. provide a nexus between the preamble and the claim steps).

35 USC § 102

- 4.** The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that may form the basis for rejections set forth in this Office action:

A person shall be entitled to a patent unless --

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) The invention was described in --

(1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or

(2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a)

CLAIM REJECTIONS UNDER 35 USC § 102

- 5.** **Claim(s) 21-22** is/are rejected under 35 U.S.C. 102(b) as being anticipated by Matsuzaki et al. [US 6,333,179 (2000)].

Claim 21 is drawn to method for amplifying nucleic acid comprising two steps: to begin, a plurality of primers having sequences of nucleotides that are different from each other and having modules of the same melting temperature are prepared, then amplifying said nucleic acid using said plurality of primers with PCR in one vessel.

Matsuzaki et al. teach a method for amplifying nucleic acid comprising the two steps and all of the limitations of Claim 21. For example, look at the primer pairs for exon 4 (i.e. SEQ ID NOs: 5-6) and exon 7 (i.e. SEQ ID NOs: 11-12). In the primer pairs used to amplify exon 4 and exon 7 the examiner considers the modules to be the 5' G nucleotides on SEQ ID NOs: 5-6 and SEQ ID NOs: 11-12. As all of the oligos listed herein have modules comprising a single G nucleotide at their 5' terminals, all of the modules will have the same melting temperatures. Beyond the modules, note that SEQ ID NOs: 5-6 and 11-12 comprise a sequences of nucleotides that are different from each other.

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Claim 22 is drawn to an embodiment of Claim 21 wherein said modules have the same length and the same compositions of nucleotides.

As argued above against Claim 21, Matsuzaki et al. teach a method for amplifying nucleic acid comprising the two steps and all of the limitations of Claim 22.

35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

7. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligations under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103.

CLAIM REJECTIONS UNDER 35 USC § 102/103

8. **Claim(s) 17, and 19-20, 24-26** is/are rejected under 35 U.S.C. 102(e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Matsuzaki et al. [US 6,333,179 (2000)].

Claim 17 is drawn to a method for amplifying NA comprising three steps. To begin, a first primer is prepared which has a first sequence of nucleotides and a first module. Next, a second primer is prepared which has a second sequence of nucleotides and a second module. Finally, the first and second primers are used to amplify said NA via PCR in a single tube wherein the first and the second

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nucleotide sequences are different and wherein the reaction efficiency of the first module in the PCR reaction and the reaction efficiency of the second module in the PCR reaction are substantially the same because the melting temperature of both the first and the second modules are substantially the same.

Matsuzaki et al. teach a method for amplifying NA comprising all of the limitations of Claim 17. For example, look at the primer pairs for exon 2 (i.e. SEQ ID NOs: 1-2) and exon 9 (i.e. SEQ ID NOs: 15-16). In the primer pair used to amplify exon 2 (i.e. SEQ ID NOs: 1-2) the examiner considers the first module to be the 5' T nucleotide on SEQ ID NO: 1 and the second module to be the 5' T nucleotide on SEQ ID NO: 2. Beyond the modules, note that SEQ ID NO: 1 comprises a sequence of nucleotides that is different from the sequence of nucleotides comprising SEQ ID NO: 2.

In the primer pair used to amplify exon 9 (i.e. SEQ ID NOs: 15-16) the examiner considers the first module to be the ACTTT near the 5' end of SEQ ID NO: 15 and the second module to be the ACTTT near the 5' end of SEQ ID NO: 16. Beyond the modules, note that SEQ ID NO: 15 comprises a sequence of nucleotides that is different from the sequence of nucleotides comprising SEQ ID NO: 16. Note that SEQ ID NO: 15 comprises a sequence of nucleotides that is different from the sequence of nucleotides comprising SEQ ID NO: 16.

| | |
|---------------|---|
| SEQ ID NO: 1 | 5' - <u>TCATGCTGGATCCCCACTTTTCCTCTTG</u> -3' (28 - mer) |
| SEQ ID NO: 2 | 5' - <u>TGGCCTGCCCTTCCAATGGTCCACTCA</u> -3' (27 - mer) |
| SEQ ID NO: 15 | 5' - <u>CACTTTTATCACCTTTCCTTGCCTCTTTCC</u> -3' (30 - mer) |
| SEQ ID NO: 16 | 5' - <u>AACTTTCCACTTGATAAGAGGTCCCAAGAC</u> -3' (30 - mer) |

The module for each primer is shown in bold print while the nucleotide sequence of each oligo is underlined

Note, that in this interpretation, the PCR reaction efficiencies of the first module and the second modules of the exon 2 primer pair should be substantially the same as their melting temperatures should be substantially the same. The same is true the modules of the primers that amplify exon 9 (i.e. SEQ ID NOs: 15-16)

Admittedly, Matsuzaki et al. do not teach that the reaction efficiencies of the first and second modules are substantially the same in the PCR reaction because the melting temperature of both the first and second modules are substantially the same. However, absent a showing to the contrary, this limitation is considered to be inherent to the PCR primers taught by Matsuzaki et al. Note that the two modules of both of the primer pairs listed above have exactly the same sequence and therefore have exactly the same melting temperatures.

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Claim 19 is drawn to an embodiment of Claim 17 wherein said first module and the second module have substantially the same length.

Matsuzaki et al. teach this limitation. See, for example, the diagram above which shows a schematic of the first and the eighth primer pairs listed in Table 1. As regards the first primer pair both of these oligos (i.e. SEQ ID NOs: 1-2) have a single T at their 5' terminals. If one defines a "module" as a single nucleotide on the 5' end of the oligo then said first module and the second module have substantially the same length (i.e. one nucleotide). The same is true for the eighth primer pair listed in Table 1 (i.e. SEQ ID NOs: 15-16). As regards the eighth primer pair both of these oligos (i.e. SEQ ID NOs: 15-16) have ACTTT module at their 5' terminals. If one defines a "module" as a run of five nucleotides at the 5' end of an oligo, then the first module and the second module in the eighth primer pair listed in Table 1 (i.e. SEQ ID NOs: 15-16) have substantially the same length (i.e. five nucleotides).

Claim 20 is drawn to an embodiment of Claim 17 wherein both the first module and the second module comprise a set of modules having the same composition of nucleotides.

Matsuzaki et al. teach this embodiment. See, for example, the diagram above which shows a schematic of the first and the eighth primer pairs listed in Table 1. Note that the composition of the first module and the second modules are identical if you consider the first primer to be SEQ ID NO: 1 and the second primer to be SEQ ID NO: 2.

Claim 24 is drawn to an embodiment of Claim 17 wherein said nucleic acid is double stranded. **Claim 25** is drawn to an embodiment of Claim 17 wherein said nucleic acid is DNA.

Matsuzaki et al. teach these embodiments wherein these authors teach "the method comprises priming DNA synthesis on a genomic p53 template in a vessel with ten sets of primers which amplify exons 2-11 of p53." Note that genomic DNA is double stranded prior to its denaturation during the PCR assay.

Claim 26 is drawn to an embodiment of Claim 17 wherein the lengths of said first and second primers are the same. Matsuzaki et al. teach this embodiment wherein these authors teach that the primers for exon 9 (i.e. SEQ ID NOs: 15 and 16) are both 30 -mers (i.e. the lengths of said first and second primers are the same).

CLAIM OBJECTIONS

9. **Claim(s) 23** is /are objected to as being dependent upon a rejected base claim.

RESPONSE TO APPLICANT'S AMENDMENT/ ARGUMENTS

10. Applicant's arguments with respect to the claimed invention have been fully and carefully considered but are moot in view of the new ground(s) of rejection.

CONCLUSION

11. Claim(s) 17 and 19-26 is/are rejected and/or objected to for the reason(s) set forth above.

12. Applicant's amendment necessitated the new grounds of rejection. Accordingly, **THIS ACTION IS MADE FINAL.** See M.P.E.P. § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. § 1.136(a).

A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. § 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ethan Whisenant, Ph.D. whose telephone number is (703) 308-6567. The examiner can normally be reached Monday-Friday from 8:30AM -5:30PM EST or any time via voice mail. If repeated attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached at (703) 308-1152.

The fax number for this Examiner is (703) 746-8465. Before faxing any papers please inform the examiner to avoid lost papers. Please note that the faxing of papers must conform with the Notice to Comply published in the Official Gazette, 1096 OG 30 (November 15, 1989). Any inquiry of a general nature or relating to the status of this application should be directed to the group receptionist whose telephone number is (703) 308-0196.



**ETHAN WHISENANT
PRIMARY EXAMINER**